releasing hormone (CRH), [a somatostatin polypeptide analogue] a biologically active analogue of somatostatin, [a gonadotropin agonist polypeptide analogue (GnRHa)] a biologically active analogue of gonadotropin agonist, human atrial natriuretic peptide (hANP), recombinant human thyroxine releasing hormone (TRHrh), follicle stimulating hormone (FSH), or prolactin.

REMARKS

Claims 1-22 and 26-60 remain pending. The above amendments to claims 1 and 21 are supported in the specification by disclosure concerning how the claimed compositions can be manufactured. In the processes described on pages 16-17, carryover paragraph, the enhancer compound (as well as the polypeptide) must be of a consistency that permits it to be processed into particles of a size under 10 microns. Claims 4 and 27 are amended in accordance with the Examiner's suggestion, to more clearly indicate the claimed invention. The replacement of Table I on page 22 of the specification with the new Table I in Appendix 1 merely corrects formatting errors in the original (the misspelled word at line 10 having already been corrected in the July 18 Office Action, paragraph 2). No new matter was added by this amendment.

Applicants thank Examiner Duffy for the courteous and helpful telephonic interview with the undersigned on January 12, 1998. During this interview, the above claim amendments as well as the evidence and arguments submitted with the March 27, 1997

response were discussed. The Examiner indicated in the interview that the amendments appeared to be acceptable.

In the pending office action (mailed July 18, 1997, by then-Examiner Prickril), the extensive evidence and arguments submitted by Applicants in the response filed March 27, 1997, were largely ignored, and the outstanding rejections were repeated essentially without modification. These rejections are discussed below.

35 USC §112, ¶2

Claims 4 and 27 were rejected as indefinite because they utilized the terms "vasopressin polypeptide analogue", "somatostatin polypeptide analogue", and "gonadotropin agonist polypeptide analogue". At the suggestion of Examiner Duffy, these terms have been amended to specify "biologically active" analogs; "polypeptide" has been deleted as redundant since claims 4 and 27 depend from claims that require that the compound be a polypeptide. As illustrated in the evidence submitted as Exhibit A with the March 27, 1997 response, "analog" in the very limited context used herein is understood by those of ordinary skill in the art to denote particular, known compounds. The modifier "biologically active" is consistent with this. During the interview of January 12, Examiner Duffy noted this and indicated that the rejection of these claims as indefinite would be withdrawn upon filing of the amendment.

Claim 12 stands rejected by Examiner Prickril as indefinite because of the terms "bile salt derivative" and "cyclodextrin or derivative thereof." In the telephonic interview of January 12, Examiner Duffy agreed with Applicants that the evidence submitted with the March 27, 1997 response concerning the latter term was adequate to overcome the indefiniteness rejection, although a full cite for the submitted pages was requested. The cite is Cyclodextrin Technology, Topics in Inclusion Science, by Jozsef Szejtli (Kluwer Academic Publishers, The Netherlands), 1988, ISBN 90-277-2314-1.

That the term "bile salt derivative" is understood by those in the pharmaceutical arts is evidenced by the use of the term in each of the references attached as Appendix 2, 3 and 4, respectively. Appendix 2 is two pages from Lee, Journal of Controlled Release 13:213-223, 1990. See the reference to "bile salts...and their derivatives" on page 215, column 2, last paragraph. Appendix 3 is Mattson et al., US Patent No. 5,085,868: see the reference to "bile salts or derivatives thereof" at column 5, line 9. Appendix 4 is Lee et al., US Patent No. 5,534,496: see the reference to "bile salts and derivatives" at column 2, lines 4-5. Withdrawal of the rejections under §112, ¶2, is respectfully requested.

35 USC §§102(e) and 103

Examiner Prickril's Office Action reasserted the rejection of a number of the claims as anticipated and/or obvious

over Platz et al. (U.S. Patent No. 5,284,656), in spite of the amendments and arguments filed by Applicants with the March 27, 1997 response. In the telephonic interview of January 12, 1998, Examiner Duffy indicated that in view of the teachings of Platz et al. concerning the oily or waxy types of surfactants that should be used to keep insulin particles suspended in propellant, the "non-waxy solid" limitation added to the claims in the prior amendment appeared to be sufficient to overcome this rejection. Furthermore, since the oily or waxy compounds taught by Platz et al. cannot be successfully processed into primary particles less than 10 microns in diameter, Examiner Duffy agreed that the newly substituted limitation "which has a consistency that permits it to be processed into primary particles having a diameter less than 10 microns" also succeeds in overcoming the rejection over Platz et al.

For the same reasons, the same limitation also distinguishes the present invention from the compositions disclosed by Rubsamen (US Patent No. 5,364,838), even taken in view of Platz et al. or the Clark et al., Edman et al., and Mishima et al. references cited in the Office Action. As argued at length in the March 27, 1997, response, neither Platz et al. nor Rubsamen discloses a dry powder composition for inhalation from a dry powder inhaler that includes anything that could be deemed an absorption enhancer. Platz et al. teaches that absorption enhancers are <u>unnecessary</u> to achieve pulmonary absorption of a polypeptide (col.2, lines 56-60); Rubsamen goes

even farther, teaching that it not only is unnecessary, but also should be avoided (col.2, lines 57-59). Because Platz et al. and Rubsamen teach away from the present invention, they cannot be said to render it obvious.

During the January 12 telephonic interview, Examiner Duffy noted that she agreed with Applicants' arguments and intended to withdraw the pending rejections over the prior art.

Applicant submits that all of the claims are now in condition for allowance, which action is requested. Filed herewith is a Petition for Automatic Extension with the required fee. Please charge any additional fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

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